ATTACHMENT TO AMENDMENT AND REPLY PURSUANT TO 37 C.F.R. §1.111
DATED JUNE 17, 2002

# EXHIBIT 1

# Trinity College Dublin Spin-Off Eyes Dominant Genetic Diseases

**By Cormac Sheridan**
***BioWorld International* Correspondent**

DUBLIN, Ireland – One of Ireland's most successful life sciences research groups is spinning off a start-up company, Optigen Technologies Ltd., to develop therapeutic strategies for treating dominant genetic diseases.

The ocular genetics research unit, based at the Smurfit Genetics Institute at Trinity College Dublin (TCD), has built up a strong track record over the past 15 years in the molecular genetics of retinitis pigmentosa (RP), a set of inherited degenerative conditions affecting the retina that lead eventually to blindness. It was at the forefront of efforts to map and characterize autosomal dominant forms of RP in the early 1990s. Since then, it has developed and patented a technology platform that is broadly applicable to the suppression of dominant genetic mutations.

"Recessive disease is much easier to treat," said Optigen's acting CEO, Jane Farrar, who, along with Peter Humphries and Paul Kenna, is co-director of the TCD ocular genetics group. Such conditions need the addition of a working wild-type allele, whereas dominant mutations give rise to the production of proteins with harmful physiological effects. Over 1,000 dominant conditions have been described in humans, Farrar said.

The nascent company will itself concentrate on three areas – RP, brittle bone disease and dominant tumors. It also plans to apply the platform to other conditions through joint development and outlicensing deals.

The company still is keeping the details of its platform and its therapeutic strategy under wraps. "We're very conscious that we're very small, and we need to get a lead time," Farrar said. However, its approach is based on combining gene therapy with ribozyme-based pharmaceuticals in order to suppress the pathological effects of dominant mutations.

The strength of Optigen's method lies in its potential to suppress multiple dominant mutations found in a particular allele in a non-site-specific manner. More than 150 different mutations in the rhodopsin gene can give rise to a dominant form of RP, for example, and developing individual therapies for each one is not feasible. Optigen also will look at ways of retarding apoptotic processes that accelerate the onset of RP.

The company does not yet have any people on the payroll, although an initial team of seven employees has been selected. The company is still negotiating terms with Trinity College Dublin. This process is expected to be completed early in the new year, Farrar said. Optigen then plans to raise seed funding of around EUR1.25 million, before seeking a more substantial round 12 months later. At that point, it also will look for a permanent CEO. ■

# Transgene Embarks On Second Phase II Of Therapeutic Vaccine

**By James Etheridge**
***BioWorld International* Correspondent**

PARIS – The Strasbourg-based gene therapy company Transgene SA initiated another Phase II clinical trial of its MVA-HPV-IL2 vaccine, this time in the indication of vulvar intraepithelial neoplasia (VIN3).

A Phase II trial of the same immunotherapeutic vaccine for the treatment of cervical cancer started in October. (See *BioWorld International*, Oct. 24, 2001.)

This trial is being conducted at two hospitals in the Paris area – Cochin and Ambroise Paré – and will involve up to 30 women suffering from VIN3. It will be placebo controlled and evaluate the efficacy of multiple subcutaneous injections of the MVA-HPV-IL2 vaccine. Its efficacy will be measured in terms of the elimination of lesions in at least half the treated women after six months.

VIN3 is the most severe of the three forms of vulvar intraepithelial neoplasia, a vulvar tissue disease caused by changes in the cells of the tissue that allow them to grow abnormally. In a small number of cases, VIN can evolve into invasive cancer of the vulva, and current treatments are both unpleasant for the patient and often ineffective, since relapse is common.

Transgene CEO Gilles Belanger said, "If efficacy is demonstrated in the Phase II clinical trial, we will seek orphan drug status for this indication in order to make the treatment more rapidly available to patients."

The MVA-HPV-IL2 vaccine uses the MVA vector, a highly attenuated pox virus, to express two human papillomavirus (HPV) antigens found in HPV16, the E6 and E7 proteins. The objective of treating VIN3 sufferers with MVA-HPV-IL2 is to induce an efficient immune response against HPV16 and to produce the same anti-lesion effect obtained in earlier animal studies.

Explaining the company's overall plan of campaign for this product, Belanger said, "Demonstrating the efficacy of our MVA-HPV-IL2 vaccine candidate in different stages of diseases linked to HPV infections is part of our strategy of developing this product candidate as a therapeutic vaccine."

The product has undergone Phase I clinical trials in the U.S. and Europe in which it was tested on patients suffering from various stages of cervical lesions. The trials demonstrated both the safety and tolerability of the vaccine, and provided evidence of an immune response in some patients. The Phase II trial in cervical cancer is being conducted at two centers in Mexico. ■

TGLine News
Base DATASTAR Business & Industry
09/01/2002
Identifiant : 200201000766

# *Transgene initiates Phase II trial for VIN3.*

Date : 20020107

Sous-titre :
Product is in testing for treating vulvar intra-epithelial neoplasia.

Source article :
Marketletter; Page: na; January 07, 2002; ISSN: 0951 3175; United Kingdom.

Société : TRANSGENE SA

Texte :

French biotechnology company Transgene has initiated a Phase II clinical trial of its immunotherapeutic MVA-HPV-IL2 vaccine candidate for the treatment of vulvar intra-epithelial neoplasia (VIN3).

The Phase II trial will be conducted on 30 women at two sites in France, the Ambroise Pare Hospital in Boulogne and Cochin Hospital in Paris, and will evaluate the efficacy of multiple subcutaneous injections. The trial will be placebo controlled and the primary objective is to demonstrate clinical efficacy as measured by the elimination of lesions in at least half of the treated patients at six months.

MVA-HPV-IL2 is also currently being studied in a Phase II trial for the treatment of cervical cancer. Phase I studies of MVA-HPV-IL2 conducted in the USA and Europe evaluated patients with various stages of cervical lesions. These trials demonstrated a positive safety and tolerance profile of MVA-HPV-IL2 and provided evidence of immune response in some patients.

MVA-HPA-IL2 uses the MVA vector, a highly-attenuated pox virus, to express two human papilloma virus (HPV) antigens found in HPV 16, the E6 and E7 proteins. The objective of treating VIN3 patients with MVA-HPV-IL2 is to induce an efficient immmune response against HPV 16 and to produce the anti-lesion effect that was observed in earlier animal studies.

VIN3 is the most severe of three different forms of vulvar intra-epithelial neoplasia, a vulvar tissue disease. It is caused by changes in the cells of the tissue that allow them to grow abnormally. In a small number of cases, VIN can progress to invasive cancer of the vulva. Current treatments are usually irritating to patients and relapse is frequent. Surgery is currently not used to treat VIN3 when the lesions are extensive.



THIS IS THE FULLTEXT.